

PATENT
USSN 10/674,836
Docket 082/103c

CLAIM AMENDMENTS

1. *(Currently amended)* A method of killing a mammalian cell that expresses telomerase reverse transcriptase (TERT), comprising contacting the cell with a polynucleotide in which a promoter sequence controls transcription of a transcribable sequence that the expression of which is toxic to the cell or renders the cell more susceptible to toxicity of a drug;
wherein the promoter ~~has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and~~ contains a nucleotide sequence that is at least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1 ;
and wherein the promoter causes the transcribable sequence to be expressed in cells endogenously expressing TERT.
2. *(Currently amended)* A method of killing a mammalian cell that expresses telomerase reverse transcriptase (TERT), comprising contacting the cell with a polynucleotide in which a promoter sequence controls transcription of a transcribable sequence that the expression of which is toxic to the cell or renders the cell more susceptible to toxicity of a drug;
wherein the promoter ~~has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and~~
is either
 - a) contained in the APAI-FSPI fragment just upstream of the encoding sequence for human telomerase reverse transcriptase (~~hTERT~~) TERT in lambda phage GΦ5 deposited as ATCC Accession No. 98505; or
 - b) comprises a nucleotide sequence that hybridizes to DNA complementary to said APAI-FSPI fragment at 5 to 10°C below T_m in aqueous solution at 1 M NaCl followed by wash in $0.2 \times \text{SSC}$, wherein T_m is the melting temperature of the APAI-FSPI fragment in double-stranded form ;and wherein the promoter causes the transcribable sequence to be expressed in cells endogenously expressing TERT.
3. *(Currently amended)* The method of claim 2, ~~which~~ wherein said promoter hybridizes to lambda phage GΦ5 at 5°C below T_m in aqueous solution at 1 M NaCl.
4. *(Original)* The method of claim 2, wherein the promoter contains a nucleotide sequence that is at least 80% identical to the sequence from position -239 to position -36 from the translation initiation site of SEQ. ID NO:1.

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5. *(Original)* The method of claim 1, wherein the promoter contains a nucleotide sequence that is at least 95% identical to the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
6. *(Currently amended)* The method of claim 1, wherein the promoter contains the sequence from ~~position -147~~ position -239 to position -36 from the translation initiation site of SEQ. ID NO:1.
7. *(Original)* The method of claim 1, wherein the promoter contains the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
8. *(Original)* The method of claim 1, wherein the promoter is between about 400 to 900 nucleotides in length.
9. *(Original)* The method of claim 1, wherein the promoter is between about 200 to 400 nucleotides in length.
10. *(Original)* The method of claim 1, wherein the promoter is between about 100 to 200 nucleotides in length.
11. *(Currently amended)* The method of claim 1, wherein the transcribable sequence encodes a protein selected from ~~the group consisting of~~ ricin, diphtheria toxin, other polypeptide toxins, ~~thymidine kinase, and an enzyme that induces~~ and enzymes that induce apoptosis.
12. CANCELLED
13. *(Original)* The method of claim 1, wherein the polynucleotide is an adenovirus vector.
14. *(Original)* The method of claim 1, wherein the cell is a cancer cell.

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15. *(Currently amended)* A method of treating cancer in a subject, comprising contacting cancer cells in the subject that express TERT with a polynucleotide in which a promoter sequence controls transcription of a transcribable sequence that the expression of which is toxic to the cell or renders the cell more susceptible to toxicity of a drug;

wherein the promoter ~~has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and~~ contains a nucleotide sequence that is at least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1 ;

and wherein the promoter causes the transcribable sequence to be expressed in cells endogenously expressing TERT.

16. *(Currently amended)* A method of expressing a transcribable nucleotide sequence in a mammalian cell expressing TERT, comprising contacting the cell with a polynucleotide in which the transcribable nucleotide sequence is operably linked to a promoter sequence ~~so as to cause it to be transcribed when the polynucleotide is in cells endogenously expressing human telomerase reverse transcriptase (hTERT);~~

wherein the promoter ~~has the property of causing the transcribable sequence to be expressed in cells endogenously expressing TERT, and~~ contains a nucleotide sequence that is at least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1 ;

and wherein the promoter causes the transcribable sequence to be expressed in cells endogenously expressing TERT.

17. CANCELLED

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18. (*Currently amended*) A polynucleotide in which a promoter is operably linked to a heterologous sequence ~~so as to cause the heterologous sequence to be transcribed when the polynucleotide is in cells endogenously expressing human telomerase reverse transcriptase (hTERT);~~
wherein the promoter is either
a) contained in the APAI-FSPI fragment just upstream of the encoding sequence for ~~human telomerase reverse transcriptase (hTERT)~~ human TERT in lambda phage GΦ5 deposited as ATCC Accession No. 98505; or
b) comprises a nucleotide sequence that hybridizes to DNA complementary to said APAI-FSPI fragment at 5 to 10°C below T_m in aqueous solution at 1 M NaCl followed by wash in $0.2 \times \text{SSC}$, wherein T_m is the melting temperature of the APAI-FSPI fragment in double-stranded form and wherein the promoter causes the heterologous sequence to be expressed in cells endogenously expressing TERT.
19. (*Original*) The polynucleotide of claim 18, which hybridizes to lambda phage GΦ5 at 5°C below T_m in aqueous solution at 1 M NaCl.
20. (*Original*) The polynucleotide of claim 18, wherein the promoter contains a nucleotide sequence that is at least 80% identical to the sequence from position -239 to position -36 from the translation initiation site of SEQ. ID NO:1.
21. (*New*) The method of claim 16, wherein the promoter contains the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
22. (*New*) The method of claim 16, wherein expression of the transcribable nucleotide sequence renders the cell more susceptible to toxicity of a drug.
23. (*New*) The method of claim 22, wherein the transcribable nucleotide sequence is thymidine kinase.
24. (*New*) The method of claim 22, wherein the drug is ganciclovir.
25. (*New*) A method of killing a mammalian cell that expresses TERT, comprising rendering a mammalian cell that expresses telomerase reverse transcriptase (TERT) more susceptible to toxicity of a drug according to the method of claim 22, and then contacting the cell with said drug.

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26. (New) A method of killing a mammalian cell that expresses TERT and that has been rendered more susceptible to toxicity of a drug according to the method of claim 22, comprising contacting the cell with said drug.
27. (New) The method of claim 26, wherein the promoter contains a nucleotide sequence that is at least 80% identical to the sequence from position -239 to position -36 from the translation initiation site of SEQ. ID NO:1.
28. (New) The method of claim 26, wherein the promoter contains the sequence from position -117 to position -36 from the translation initiation site of SEQ. ID NO:1.
29. (New) The method of claim 26, wherein the cell is a cancer cell.
30. (New) A method of treating cancer in a subject, comprising rendering cancer cells in the subject more susceptible to toxicity of a drug according to the method of claim 22, and then contacting the cells with said drug.
31. (New) A method of rendering a mammalian cell that expresses TERT more susceptible to toxicity of a drug, comprising contacting the cell with a polynucleotide in which a promoter controls transcription of a sequence that encodes thymidine kinase;
wherein the promoter contains a nucleotide sequence that is at least 90% identical to the sequence from position -117 to position -36 from the translation initiation site (position 13545) of SEQ. ID NO:1;
and wherein the promoter causes the transcribable sequence to be expressed in cells endogenously expressing TERT.
32. (New) A method of treating cancer in a subject, comprising rendering cancer cells in the subject more susceptible to toxicity of a drug according to the method of claim 31, and then administering ganciclovir to the subject.